

### **REMARKS**

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

#### **Pending Claims**

Prior to this Amendment, Claims 1-3 were pending. Applicants assume that Claim 3 is allowable if rewritten in an independent form because the Examiner did not reject to Claim 3.

Claim 1 was amended. New Claims 9-41 are added by this Amendment.

#### **Incorporation by reference**

Consistent with the guidelines in MPEP §608(p), Applicants are adding material from WO 98/51325 to the specification. WO 98/51325 is a published application that was incorporated by reference into the present application as can be seen from the following 2 excerpts from the present application:

As disclosed and claimed in WO 98/51325, which reference is hereby incorporated by reference in its entirety, we have identified random peptides and their fragments, motifs, derivatives or peptidomimetics thereof which are capable of specific binding to GIT receptors such as the D2H, hSI, HPT1 and hPEPT1 receptors (hereinafter "GIT targeting agents"). (From page 2, lines 26-29 to page 3, lines 1-2).

Additional GIT targeting agents are disclosed throughout the above referenced WO 98/51325 (From page 6, line 1-2).

Material incorporated by reference from WO 98/51325 is summarized in the following Table 1:

TABLE 1

Material	Location in WO 98/51325	Insert position in specification of present application	Claims in which Material appears in application
Information on GIT receptors	page 45 line 25 to page 46, line 37	Page 6, after line 2	1-41
Sequences of 55 receptor-binding peptides identified from a phage library (SEQ ID NOS: 17-71)	page 54, lines 5 to page 55, lines 37	Immediately following above insert	10, 11, 12, 13, 19, 20, 21, 22, 28, 29, 30, 31, 37, 38, 39, and 40
Sequences of 13 binding motifs (SEQ ID NOS 72-84)	Claims 6, 10, 14, 18-20  Sequence Listing SEQ ID NOS: 253-265	Sequence Listing	14, 23, 32, and 41
Sequences of 4 GIT receptors (SEQ ID NOS: 13-16)	Sequence Listing SEQ ID NOS: 181, 179, 178, and 176	Sequence Listing	9, 10, 11, 12, 13, 14, 18, 19, 20, 21, 22, 23, 27, 28, 29, 30, 31, 36, 37, 38, 39, and 40.

### **Changes made in text incorporated by reference**

Applicants have incorporated text from page 45, line 25 to page 46, line 36 of WO 98/51325. The following changes were made:

1) Moved the title of the table, " TARGET BINDING PHAGE INSERT SEQUENCES" to become the header to the right column : --TARGET BINDING PHAGE INSERT SEQUENCE--

2) Changed the SEQ ID NOS from 1-55 to 17-71.

3) Changed the SEQ ID NOS from 176,178,179, and 181 to 16, 15, 14, and 13 respectively.

4) Changed the SEQ ID NOS from 253-265 to 72-84.

5) In the section titled "6.2. Cloning of Extracellular Domain of Selected Receptor Site" removed "6.2." from the title and added a section titled "SEQ ID NOS."

### **Support for Amendments**

The following examples of support for any given claim amendment are intended to be illustrative, not exhaustive.

#### **Support for amendments to Claim 1**

Support for amendments to Claim 1 can be found in the application as filed starting on Page 2, line 26 through Page 4 line 4 wherein GIT targeting agents are defined and further on Page 5, lines 19-26 through Page 6 line 2.

#### **Support for new Claims 9-41**

New Claims 9-41 are supported generally by the application as filed and specifically, by the material incorporated by this Amendment (See Table 1 above).

New Claims 24-41 parallel claims 1-3 and 9-23, with the difference that independent

Claim 24 has different language than Claim 1 has.

Support for newly added amino acid sequences

The SEQ ID NOs of newly added sequences incorporated by reference from WO 98/51325 are presented in Table 2 below together with their corresponding SEQ ID NOs from WO 98/51325.

TABLE 2

SEQ ID NOs in present application	SEQ ID NOs in WO 98/51325	Nature of peptide/protein
17-71	1-55	Targeting agents
72-84	253-265	Targeting agents
16	176	hPEPT1 receptor
15	178	HPT1 receptor
14	179	hSI receptor
13	181	D2H receptor

**Appendix to this Amendment**

Applicants have attached an Appendix with copies of those pages from the WO 98/51325 that have the material that was incorporated via the present Amendment into the present application.

**Sequence Listing**

A "Transmittal of Sequence Listing and Related Amendment" is being co-submitted with this Amendment in view of the additional sequences added by this Amendment.

**Response to Rejections in Office Action of July 5, 2002.**

**Rejection of Claims 1 and 2 under 35 U.S.C. 112, first paragraph (Page 2 of the Office Action)**

The Examiner has rejected Claims 1 and 2 under 35 U.S.C. §112, first paragraph, as being indefinite for failing to particularly point out and claim the subject matter of the invention, specifically for failing to define "GIT." In response, Applicants have defined GIT.

**Rejection of Claims 1 and 2 under 35 U.S.C. 102(b) (Page 2 of the Office Action)**

The Examiner has rejected Claims 1 and 2 under 35 U.S.C. §102(b) as being anticipated by two references by Lobie et al. Applicants respectfully traverse this rejection.

Lobie et al (1993) teaches producing an antibody to the rabbit mammary gland prolactin receptor . Lobie et al (1990) teaches producing an antibody to the growth hormone receptor.

Neither of the two Lobie et al references teach an antibody against a protein which binds to a receptor (such as a GIT transport receptor). Therefore, neither Lobie et al reference anticipates Applicants' claimed inventions.

In view of the foregoing remarks, it is respectfully submitted that all of the claims now pending in this application are allowable.

October 3, 2002

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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

1. (Amended) An antibody or antibody fragment specific to a domain of a gastro-intestinal tract (GIT) targeting agent, said targeting agent comprising a protein that specifically binds to a GIT receptor.

**Appendix with pages from WO 98/512325**

The following pages are attached:

45-46

54-55

179-180

184-189

192-194

234-237

Material incorporated by reference into the present application is marked by a vertical black line in the right margins.

form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient.

The Therapeutics of the invention can be formulated as neutral or salt forms. Pharmaceutically acceptable salts include those formed with free amino groups such as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, etc., and those formed with free carboxyl groups such as those derived from sodium, potassium, ammonium, calcium, ferric hydroxides, isopropylamine, triethylamine, 2-ethylamino ethanol, histidine, procaine, etc.

The amount of the Therapeutic of the invention which will be effective in the treatment of a particular disorder or condition will depend on the nature of the disorder or condition, and can be determined by standard clinical techniques. In addition, *in vitro* assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the formulation will also depend on the route of administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances.

## 6. EXAMPLES

### 25 6.1. Selection of GIT Receptor Targets

The HPT1, hPEPT1, D2H, and hSI receptors were selected for cloning as GIT receptor targets based on several criteria, including: (1) expression on surface of epithelial cells in gastro-intestinal tract (GIT); (2) expression along the length of small intestine (HPT1, hPEPT1, D2H); (3) expression locally at high concentration (hSI); (4) large putative extracellular domains facing into the lumen of the GIT; and (5) extracellular domains that permit easy access and bioadhesion by targeting particles.

35 The four recombinant receptor sites screened with the peptide libraries additionally have the following characteristics:

	<u>Receptor</u>	<u>Characteristics</u>
	D2H	Transport of neutral/basic amino acids; a transport activating protein for a range of amino acid translocases
5	hSI	Metabolism of sucrose and other sugars; represents 9% of brush border membrane protein in Jejunum
	HPT1	di/tri peptide transporter or facilitator of peptide transport
	hPEPT1	di/tri peptide transporter
10	Figures 1-4 (SEQ ID NOS:176, 178, 179, and 181, respectively) show the predicted amino acid sequences for hPEPT1, HPT1, hSI and D2H, respectively.	

#### 6.2. Cloning of Extracellular Domain of Selected Receptor Site

The following receptor domains were cloned and expressed as His-tag fusion proteins by standard techniques:

	<u>Receptor</u>	<u>Domain (amino acid residues)</u>
20	hPEPT1 <sup>a</sup>	391-571
	HPT1 <sup>b</sup>	29-273
	hSI <sup>c</sup>	272-667
	D2H <sup>d</sup>	387-685

- <sup>a</sup> Liang et al., 1995, J. Biol. Chem. 270:6456-6463  
<sup>b</sup> Dantzig et al., 1994, Association of Intestinal Peptide Transport with a Protein Related to the Cadherin Superfamily  
<sup>c</sup> Chantret et al., Biochem. J. 285:915-923  
<sup>d</sup> Bertran et al., J. Biol. Chem. 268:14842-14949

The receptor proteins were expressed as His-tag fusion proteins and affinity purified under denaturing conditions, using urea or guanidine HCl, utilizing the pET His-tag metal chelate affinity for Ni-NTA Agarose (Hochuli, E., Purification of recombinant proteins with metal chelate adsorbent, Genetic Engineering, Principals and Methods (J.K. Setlow, ed.), Plenum Press, NY, Vol. 12 (1990), pp. 87-98).

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5            Phage which showed specificity to a GIT receptor was further characterized by ELISA on a variety of recombinant proteins. Phage which continued to exhibit GIT receptor specificity was sequenced.

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TARGET BINDING PHAGE INSERT SEQUENCES:

- 54 -

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DCX8	23	RYKHDIGCDAGVDKKSSSVRGCGAHSSPPRAGRGRGTMTVSRL
DCX11	24	SQGSKQCMQYRTGRLTVGSEYGCGMNPARGHATPAYPARLLPRYR
DCX26	25	SGRTTSEISGLWGWGDDRSYGWGNLTPNYIPYRQATNRHRYT
DCX33	26	RWNWTVLPATGGHYWTRSTDYHAINNHRPSIPHQHPTPI
5 DCX36	27	SWSSWNWSSKTTRLGDRATREGCGPSQSDGCPYNGRLTTVKPRT
DCX39	28	SGSLNAWQPRSWVGGAFRSHANNLNPKPTMVTRHPT
DCX42	29	RYSGLSPRDNGPACSQEATLEGCGAQLMSTRRKGRNSRPGWTL
DCX45	30	SVGNDKTSRPVSFYGRVSDLWNASLMPKRTPPSSKRHDDG

10 hPEPT1

PAX9	31	RWPSVGKNGSDTIDVHSNDASTKRSLIYNHRRPLFP
PAX14	32	RTFENDGLGVGRSIQKSDRWYASHNIRSHFASMSPAGK
PAX15	33	SYCRVKGGEGGHTDSNLARSGCGKVARTSRLQHINPRATPPSR
PAX16	34	SWTRWGKHTHGGFVNKSPPGKNATSPYTDAQLPSDQGGP
15 PAX17	35	SQVDSFRNSFRWYEPSRALCHGCGKRDSTTRIHNSPSDSYPTR
PAX18	36	SFLRFQSPRFEDYSRTISRLRNATNPSNVSDAHNNRALA
PAX35	37	RSITDGGINEVDLSSVSNVLENANSHRAYRKHRTPLKRP
PAX38	38	SSKVSSPRDPTVPRKGGNVGYGCGHRSSARMPTSALSSITKCYT
PAX40	39	RASTQGGRGVAPEFGASVLGRGCGSATYYTNSTCKDAMGHNYS
20 PAX43	40	RWCEKHKFTAARCSAGAGFERDASRPPQPAHRDNTNRNA
PAX45	41	SFQVYPDHGLERHALDGTGPLYAMPGRWIRARPQNRDRQ
PAX46	42	SRCTDNEQCPDTGTRSRSVSNARYFSSRLLKTHAPHRP
P31	43	SARDSGPAEDGSRVRLNGVENANTRKSSRSNPRGRRHP
P90	44	SSADAEEKCAGSLLWWGRQNNSGCGSPTKKHLKHNRSQTSSSSH
25 5PAX3	45	RPKNVADAYSSQDGAEEETSHASNAARKSPKHKLRRP
5PAX5	46	RGSTGTAGGERSGVLNLHTRDNASGSGFKPWYPSNRGHK
5PAX7	47	RWGWERSPSDYDSMDLGARRYATRTHRAPPVRLKAPLP
5PAX12	48	RGWKCEGSQAAYGDKDIGRSRGCSITKNNTNHAHPHSHGAVAKI

30 HPT-1

HAX9	49	SREEANWDGYKREMSHRSRFWDATHLSRPRRPANSGDPN
HAX35	50	EWYSWKRSSKSTGLGDTATREGCGPSQSDGCPYNGRLTTVKPRK
HAX40	51	REFAERRLWGCDDLSWRLDAEGCGPTPSNRAVKHRKPRPRSPAL
HAX42	52	SDHALGTNLRSDNAKEPGDYNCCGNGNSTGRKVFNRRRPSAIP
35 HCA3	53	RHISEYSFANSHLMGGESKRKCGGINGSFSPTCPRSPTPAFRRT
H40	54	SRESGMWGSWWRGHRLNSTGGNANMNASLPPDPPVSTP
PAX2	55	STPPSREAYSRPYSVSDSDTNAKHSSHNRLRLTRSRPN

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 10 amino acids  
 (B) TYPE: amino acid  
 (C) STRANDEDNESS:  
 (D) TOPOLOGY: unknown

## (ii) MOLECULE TYPE: peptide

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## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:175:

Arg Arg Leu Arg Thr Arg Ser Arg Pro Asn  
 1 5 10

## (2) INFORMATION FOR SEQ ID NO:176:

10

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 708 amino acids  
 (B) TYPE: amino acid  
 (C) STRANDEDNESS:  
 (D) TOPOLOGY: unknown

## (ii) MOLECULE TYPE: peptide

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:176:

15 Met Gly Met Ser Lys Ser His Ser Phe Phe Gly Tyr Pro Leu Ser Ile  
 1 5 10 15  
 Phe Phe Ile Val Val Asn Glu Phe Cys Glu Arg Phe Ser Tyr Tyr Gly  
 20 25 30  
 Met Arg Ala Ile Leu Ile Leu Tyr Phe Thr Asn Phe Ile Ser Trp Asp  
 35 40 45  
 Asp Asn Leu Ser Thr Ala Ile Tyr His Thr Phe Val Ala Leu Cys Tyr  
 50 55 60  
 Leu Thr Pro Ile Leu Gly Ala Leu Ile Ala Asp Ser Trp Leu Gly Lys  
 65 70 75 80  
 20 Phe Lys Thr Ile Val Ser Leu Ser Ile Val Tyr Thr Ile Gly Gln Ala  
 85 90 95  
 Val Thr Ser Val Ser Ser Ile Asn Asp Leu Thr Asp His Asn His Asp  
 100 105 110  
 Gly Thr Pro Asp Ser Leu Pro Val His Val Val Leu Ser Leu Ile Gly  
 115 120 125  
 Leu Ala Leu Ile Ala Leu Gly Thr Gly Gly Ile Lys Pro Cys Val Ser  
 130 135 140  
 25 Ala Phe Gly Gly Asp Gln Phe Glu Glu Gly Gln Glu Lys Gln Arg Asn  
 145 150 155 160  
 Arg Phe Phe Ser Ile Phe Tyr Leu Ala Ile Asn Ala Gly Ser Leu Leu  
 165 170 175  
 Ser Thr Ile Ile Thr Pro Met Leu Arg Val Gln Gln Cys Gly Ile His  
 180 185 190  
 Ser Lys Gln Ala Cys Tyr Pro Leu Ala Phe Gly Val Pro Ala Ala Leu  
 195 200 205  
 Met Ala Val Ala Leu Ile Val Phe Val Leu Gly Ser Gly Met Tyr Lys  
 210 215 220  
 30 Lys Phe Lys Pro Gln Gly Asn Ile Met Gly Lys Val Ala Lys Cys Ile  
 225 230 235 240  
 Gly Phe Ala Ile Lys Asn Arg Phe Arg His Arg Ser Lys Ala Phe Pro  
 245 250 255  
 Lys Arg Glu His Trp Leu Asp Trp Ala Lys Glu Lys Tyr Asp Glu Arg  
 260 265 270  
 Leu Ile Ser Gln Ile Lys Met Val Thr Arg Val Met Phe Leu Tyr Ile  
 275 280 285  
 35 Pro Leu Pro Met Phe Trp Ala Leu Phe Asp Gln Gln Gly Ser Arg Trp  
 290 295 300  
 Thr Leu Gln Ala Thr Thr Met Ser Gly Lys Ile Gly Ala Leu Glu Ile  
 305 310 315 320  
 Gln Pro Asp Gln Met Gln Thr Val Asn Ala Ile Leu Ile Val Ile Met

325 330 335  
 Val Pro Ile Phe Asp Ala Val Leu Tyr Pro Leu Ile Ala Lys Cys Gly  
 340 345 350  
 Phe Asn Phe Thr Ser Leu Lys Lys Met Ala Val Gly Met Val Leu Ala  
 355 360 365  
 Ser Met Ala Phe Val Val Ala Ala Ile Val Gln Val Glu Ile Asp Lys  
 370 375 380  
 5 Thr Leu Pro Val Phe Pro Lys Gly Asn Glu Val Gln Ile Lys Val Leu  
 385 390 395 400  
 Asn Ile Gly Asn Asn Thr Met Asn Ile Ser Leu Pro Gly Glu Met Val  
 405 410 415  
 Thr Leu Gly Pro Met Ser Gln Thr Asn Ala Phe Met Thr Phe Asp Val  
 420 425 430  
 Asn Lys Leu Thr Arg Ile Asn Ile Ser Ser Pro Gly Ser Pro Val Thr  
 435 440 445  
 10 Ala Val Thr Asp Asp Phe Lys Gln Gly Gln Arg His Thr Leu Leu Val  
 450 455 460  
 Trp Ala Pro Asn His Tyr Gln Val Val Lys Asp Gly Leu Asn Gln Lys  
 465 470 475 480  
 Pro Glu Lys Gly Glu Asn Gly Ile Arg Phe Val Asn Thr Phe Asn Glu  
 485 490 495  
 Leu Ile Thr Ile Thr Met Ser Gly Lys Val Tyr Ala Asn Ile Ser Ser  
 500 505 510  
 Tyr Asn Ala Ser Thr Tyr Gln Phe Pro Ser Gly Ile Lys Gly Phe  
 515 520 525  
 15 Thr Ile Ser Ser Thr Glu Ile Pro Pro Gln Cys Gln Pro Asn Phe Asn  
 530 535 540  
 Thr Phe Tyr Leu Glu Phe Gly Ser Ala Tyr Thr Tyr Ile Val Gln Arg  
 545 550 555 560  
 Lys Asn Asp Ser Cys Pro Glu Val Lys Val Phe Glu Asp Ile Ser Ala  
 565 570 575  
 Asn Thr Val Asn Met Ala Leu Gln Ile Pro Gln Tyr Phe Leu Leu Thr  
 580 585 590  
 Cys Gly Glu Val Val Phe Ser Val Thr Gly Leu Glu Phe Ser Tyr Ser  
 595 600 605  
 20 Gln Ala Pro Ser Asn Met Lys Ser Val Leu Gln Ala Gly Trp Leu Leu  
 610 615 620  
 Thr Val Ala Val Gly Asn Ile Ile Val Leu Ile Val Ala Gly Ala Gly  
 625 630 635 640  
 Gln Phe Ser Lys Gln Trp Ala Glu Tyr Ile Leu Phe Ala Ala Leu Leu  
 645 650 655  
 Leu Val Val Cys Val Val Phe Ala Ile Met Ala Arg Phe Tyr Thr Tyr  
 660 665 670  
 25 Ile Asn Pro Ala Glu Ile Glu Ala Gln Phe Asp Glu Asp Glu Lys Lys  
 675 680 685  
 Asn Arg Leu Glu Lys Ser Asn Pro Tyr Phe Met Ser Gly Ala Asn Ser  
 690 695 700  
 Gln Lys Gln Met  
 705

## (2) INFORMATION FOR SEQ ID NO:177:

- 30 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 3345 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA  
 (ix) FEATURE:
- 35 (A) NAME/KEY: Coding Sequence  
 (B) LOCATION: 88...2583  
 (D) OTHER INFORMATION:

	CAC CAG ACT GGG ATA CCC ACT GTG GGC ATG GCA GTT GGT ATA CTG CTG	2466
	His Gln Thr Gly Ile Pro Thr Val Gly Met Ala Val Gly Ile Leu Leu	
	780 785 790	
	ACC ACC CTT CTG GTG ATT GGT ATA ATT TTA GCA GTT GTG TTT ATC CGC	2514
	Thr Thr Leu Leu Val Ile Gly Ile Ile Leu Ala Val Val Phe Ile Arg	
	795 800 805	
5	ATA AAG AAG GAT AAA GGC AAA GAT AAT GTT GAA AGT GCT CAA GCA TCT	2562
	Ile Lys Lys Asp Lys Gly Lys Asp Asn Val Glu Ser Ala Gln Ala Ser	
	810 815 820 825	
	GAA GTC AAA CCT CTG AGA AGC TGAATTTGAA AAGGAATGTT TGAATTTATA TAGC	2617
	Glu Val Lys Pro Leu Arg Ser	
	830	
10	AAGTGCTATT TCAGCAACAA CCATCTCATC CTATTACTTT TCATCTAACG TGCATTATAA	2677
	TTTTTTAAAC AGATATTCCC TCTTGTCCTT TAATATTGTC TAAATATTTC TTTTTTGAGG	2737
	TGGAGTCTTG CTCTGTCGCC CAGGCTGGAG TACAGTGGTG TGATCCCAGC TCACTGCAAC	2797
	CTCCGCCTCC TGGGTTTACA TGATTCTCCT GCCTCAGCTT CCTAAGTAGC TGGGTTTACA	2857
	GGCACCCACC ACCATGCCCA GCTAATTTT GTATTTTAA TAGAGACGGG GTTTCGCCAT	2917
	TTGGCCAGGC TGGTCTTGAA CTCCTGACGT CAAGTGATCT GCCTGCCTTG GTCTCCCAAT	2977
	ACAGGCATGA ACCACTGCAC CCACCTACTT AGATATTCA TGTGCTATAG ACATTAGAGA	3037
	GATTTTTCAT TTTTCCATGA CATTTTTCCT CTCTGCAAAAT GGCTTAGCTA CTTGTGTTTT	3097
	TCCCTTTTGG GGCAAGACAG ACTCATTAAG TATTCTGTAC ATTTTTCCT TATCAAGGAG	3157
15	ATATATCAGT GTTGTCTCAT AGAACTGCCT GGATTCCATT TATGTTTTTT CTGATTCCAT	3217
	CCTGTGTCCC CTTTCATCCT GACTCCTTG GTATTTCACT GAATTTCAAA CATTTGTCAG	3277
	AGAAGAAAAA AGTGAGGACT CAGGAAAAAT AAATAAATAA AAGAACAGCC TTTTGCGGCC	3337
	GCGAATTC	3345

## (2) INFORMATION FOR SEQ ID NO:178:

## (i) SEQUENCE CHARACTERISTICS:

- 20 (A) LENGTH: 832 amino acids  
(B) TYPE: amino acid  
(C) STRANDEDNESS:  
(D) TOPOLOGY: unknown

## (ii) MOLECULE TYPE: protein

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:178:

	Met Ile Leu Gln Ala His Leu His Ser Leu Cys Leu Leu Met Leu Tyr	
25	1 5 10 15	
	Leu Ala Thr Gly Tyr Gly Gln Glu Gly Lys Phe Ser Gly Pro Leu Lys	
	20 25 30	
	Pro Met Thr Phe Ser Ile Tyr Glu Gly Gln Glu Pro Ser Gln Ile Ile	
	35 40 45	
	Phe Gln Phe Lys Ala Asn Pro Pro Ala Val Thr Phe Glu Leu Thr Gly	
	50 55 60	
	Glu Thr Asp Asn Ile Phe Val Ile Glu Arg Glu Gly Leu Leu Tyr Tyr	
	65 70 75 80	
30	Asn Arg Ala Leu Asp Arg Glu Thr Arg Ser Thr His Asn Leu Gln Val	
	85 90 95	
	Ala Ala Leu Asp Ala Asn Gly Ile Ile Val Glu Gly Pro Val Pro Ile	
	100 105 110	
	Thr Ile Glu Val Lys Asp Ile Asn Asp Asn Arg Pro Thr Phe Leu Gln	
	115 120 125	
	Ser Lys Tyr Glu Gly Ser Val Arg Gln Asn Ser Arg Pro Gly Lys Pro	
	130 135 140	
	Phe Leu Tyr Val Asn Ala Thr Asp Leu Asp Asp Pro Ala Thr Pro Asn	
35	145 150 155 160	
	Gly Gln Leu Tyr Tyr Gln Ile Val Ile Gln Leu Pro Met Ile Asn Asn	
	165 170 175	
	Val Met Tyr Phe Gln Ile Asn Asn Lys Thr Gly Ala Ile Ser Leu Thr	
	180 185 190	

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Arg Glu Gly Ser Gln Glu Leu Asn Pro Ala Lys Asn Pro Ser Tyr Asn  
 195 200 205  
 Leu Val Ile Ser Val Lys Asp Met Gly Gly Gln Ser Glu Asn Ser Phe  
 210 215 220  
 Ser Asp Thr Thr Ser Val Asp Ile Ile Val Thr Glu Asn Ile Trp Lys  
 225 230 235 240  
 Ala Pro Lys Pro Val Glu Met Val Glu Asn Ser Thr Asp Pro His Pro  
 245 250 255  
 5 Ile Lys Ile Thr Gln Val Arg Trp Asn Asp Pro Gly Ala Gln Tyr Ser  
 260 265 270  
 Leu Val Asp Lys Glu Lys Leu Pro Arg Phe Pro Phe Ser Ile Asp Gln  
 275 280 285  
 Glu Gly Asp Ile Tyr Val Thr Gln Pro Leu Asp Arg Glu Glu Lys Asp  
 290 295 300  
 Ala Tyr Val Phe Tyr Ala Val Ala Lys Asp Glu Tyr Gly Lys Pro Leu  
 305 310 315 320  
 10 Ser Tyr Pro Leu Glu Ile His Val Lys Val Lys Asp Ile Asn Asp Asn  
 325 330 335  
 Pro Pro Thr Cys Pro Ser Pro Val Thr Val Phe Glu Val Gln Glu Asn  
 340 345 350  
 Glu Arg Leu Gly Asn Ser Ile Gly Thr Leu Thr Ala His Asp Arg Asp  
 355 360 365  
 Glu Glu Asn Thr Ala Asn Ser Phe Leu Asn Tyr Arg Ile Val Glu Gln  
 370 375 380  
 Thr Pro Lys Leu Pro Met Asp Gly Leu Phe Leu Ile Gln Thr Tyr Ala  
 385 390 395 400  
 15 Gly Met Leu Gln Leu Ala Lys Gln Ser Leu Lys Lys Gln Asp Thr Pro  
 405 410 415  
 Gln Tyr Asn Leu Thr Ile Glu Val Ser Asp Lys Asp Phe Lys Thr Leu  
 420 425 430  
 Cys Phe Val Gln Ile Asn Val Ile Asp Ile Asn Asp Gln Ile Pro Ile  
 435 440 445  
 Phe Glu Lys Ser Asp Tyr Gly Asn Leu Thr Leu Ala Glu Asp Thr Asn  
 450 455 460  
 20 Ile Gly Ser Thr Ile Leu Thr Ile Gln Ala Thr Asp Ala Asp Glu Pro  
 465 470 475 480  
 Phe Thr Gly Ser Ser Lys Ile Leu Tyr His Ile Ile Lys Gly Asp Ser  
 485 490 495  
 Glu Gly Arg Leu Gly Val Asp Thr Asp Pro His Thr Asn Thr Gly Tyr  
 500 505 510  
 Val Ile Ile Lys Lys Pro Leu Asp Phe Glu Thr Ala Ala Val Ser Asn  
 515 520 525  
 Ile Val Phe Lys Ala Glu Asn Pro Glu Pro Leu Val Phe Gly Val Lys  
 530 535 540  
 25 Tyr Asn Ala Ser Ser Phe Ala Lys Phe Thr Leu Ile Val Thr Asp Val  
 545 550 555 560  
 Asn Glu Ala Pro Gln Phe Ser Gln His Val Phe Gln Ala Lys Val Ser  
 565 570 575  
 Glu Asp Val Ala Ile Gly Thr Lys Val Gly Asn Val Thr Ala Lys Asp  
 580 585 590  
 Pro Glu Gly Leu Asp Ile Ser Tyr Ser Leu Arg Gly Asp Thr Arg Gly  
 595 600 605  
 30 Trp Leu Lys Ile Asp His Val Thr Gly Glu Ile Phe Ser Val Ala Pro  
 610 615 620  
 Leu Asp Arg Glu Ala Gly Ser Pro Tyr Arg Val Gln Val Val Ala Thr  
 625 630 635 640  
 Glu Val Gly Gly Ser Ser Leu Ser Ser Val Ser Glu Phe His Leu Ile  
 645 650 655  
 Leu Met Asp Val Asn Asp Asn Pro Pro Arg Leu Ala Lys Asp Tyr Thr  
 660 665 670  
 Gly Leu Phe Cys His Pro Leu Ser Ala Pro Gly Ser Leu Ile Phe  
 675 680 685  
 35 Glu Ala Thr Asp Asp Asp Gln His Leu Phe Arg Gly Pro His Phe Thr  
 690 695 700  
 Phe Ser Leu Gly Ser Gly Ser Leu Gln Asn Asp Trp Glu Val Ser Lys  
 705 710 715 720

B

Ile Asn Gly Thr His Ala Arg Leu Ser Thr Arg His Thr Asp Phe Glu  
 725 730 735  
 Glu Arg Ala Tyr Val Val Leu Ile Arg Ile Asn Asp Gly Gly Arg Pro  
 740 745 750  
 Pro Leu Glu Gly Ile Val Ser Leu Pro Val Thr Phe Cys Ser Cys Val  
 755 760 765  
 Glu Gly Ser Cys Phe Arg Pro Ala Gly His Gln Thr Gly Ile Pro Thr  
 770 775 780  
 5 Val Gly Met Ala Val Gly Ile Leu Leu Thr Thr Leu Leu Val Ile Gly  
 785 790 795 800  
 Ile Ile Leu Ala Val Val Phe Ile Arg Ile Lys Lys Asp Lys Gly Lys  
 805 810 815  
 Asp Asn Val Glu Ser Ala Gln Ala Ser Glu Val Lys Pro Leu Arg Ser  
 820 825 830

## (2) INFORMATION FOR SEQ ID NO:179:

10

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 1827 amino acids  
 (B) TYPE: amino acid  
 (C) STRANDEDNESS:  
 (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

15

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:179:

Met Ala Arg Lys Lys Phe Ser Gly Leu Glu Ile Ser Leu Ile Val Leu  
 1 5 10 15  
 Phe Val Ile Val Thr Ile Ile Ala Ile Ala Leu Ile Val Val Leu Ala  
 20 25 30  
 Thr Lys Thr Pro Ala Val Asp Glu Ile Ser Asp Ser Thr Ser Thr Pro  
 35 40 45  
 Ala Thr Thr Arg Val Thr Thr Asn Pro Ser Asp Ser Gly Lys Cys Pro  
 50 55 60  
 20 Asn Val Leu Asn Asp Pro Val Asn Val Arg Ile Asn Cys Ile Pro Glu  
 65 70 75 80  
 Gln Phe Pro Thr Glu Gly Ile Cys Ala Gln Arg Gly Cys Cys Trp Arg  
 85 90 95  
 Pro Trp Asn Asp Ser Leu Ile Pro Trp Cys Phe Phe Val Asp Asn His  
 100 105 110  
 Gly Tyr Asn Val Gln Asp Met Thr Thr Thr Ser Ile Gly Val Glu Ala  
 115 120 125  
 25 Lys Leu Asn Arg Ile Pro Ser Pro Thr Leu Phe Gly Asn Asp Ile Asn  
 130 135 140  
 Ser Val Leu Phe Thr Thr Gln Asn Gln Thr Pro Asn Arg Phe Arg Phe  
 145 150 155 160  
 Lys Ile Thr Asp Pro Asn Asn Arg Arg Tyr Glu Val Pro His Gln Tyr  
 165 170 175  
 Val Lys Glu Phe Thr Gly Pro Thr Val Ser Asp Thr Leu Tyr Asp Val  
 180 185 190  
 Lys Val Ala Gln Asn Pro Phe Ser Ile Gln Val Ile Arg Lys Ser Asn  
 195 200 205  
 30 Gly Lys Thr Leu Phe Asp Thr Ser Ile Gly Pro Leu Val Tyr Ser Asp  
 210 215 220  
 Gln Tyr Leu Gln Ile Ser Ala Arg Leu Pro Ser Asp Tyr Ile Tyr Gly  
 225 230 235 240  
 Ile Gly Glu Gln Val His Lys Arg Phe Arg His Asp Leu Ser Trp Lys  
 245 250 255  
 Thr Trp Pro Ile Phe Thr Arg Asp Gln Leu Pro Gly Asp Asn Asn Asn  
 260 265 270  
 35 Asn Leu Tyr Gly His Gln Thr Phe Phe Met Cys Ile Glu Asp Thr Ser  
 275 280 285  
 Gly Lys Ser Phe Gly Val Phe Leu Met Asn Ser Asn Ala Met Glu Ile  
 290 295 300  
 Phe Ile Gln Pro Thr Pro Ile Val Thr Tyr Arg Val Thr Gly Gly Ile

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835 840 845  
 Tyr Thr Phe Ser Val Ser Asn Asn Thr Leu Asp Ile Val Cys Thr His  
 850 855 860  
 Ser Ser Tyr Gln Glu Gly Thr Thr Leu Ala Phe Gln Thr Val Lys Ile  
 865 870 875 880  
 Leu Gly Leu Thr Asp Ser Val Thr Glu Val Arg Val Ala Glu Asn Asn  
 885 890 895  
 5 Gln Pro Met Asn Ala His Ser Asn Phe Thr Tyr Asp Ala Ser Asn Gln  
 900 905 910  
 Val Leu Leu Ile Ala Asp Leu Lys Leu Asn Leu Gly Arg Asn Phe Ser  
 915 920 925  
 Val Gln Trp Asn Gln Ile Phe Ser Glu Asn Glu Arg Phe Asn Cys Tyr  
 930 935 940  
 Pro Asp Ala Asp Leu Ala Thr Glu Gln Lys Cys Thr Gln Arg Gly Cys  
 945 950 955 960  
 Val Trp Arg Thr Gly Ser Ser Leu Ser Lys Ala Pro Glu Cys Tyr Phe  
 965 970 975  
 10 Pro Arg Gln Asp Asn Ser Tyr Ser Val Asn Ser Ala Arg Tyr Ser Ser  
 980 985 990  
 Met Gly Ile Thr Ala Asp Leu Gln Leu Asn Thr Ala Asn Ala Arg Ile  
 995 1000 1005  
 Lys Leu Pro Ser Asp Pro Ile Ser Thr Leu Arg Val Glu Val Lys Tyr  
 1010 1015 1020  
 His Lys Asn Asp Met Leu Gln Phe Lys Ile Tyr Asp Pro Gln Lys Lys  
 025 1030 1035 1040  
 15 Arg Tyr Glu Val Pro Val Pro Leu Asn Ile Pro Thr Thr Pro Ile Ser  
 1045 1050 1055  
 Thr Tyr Glu Asp Arg Leu Tyr Asp Val Glu Ile Lys Glu Asn Pro Phe  
 1060 1065 1070  
 Gly Ile Gln Ile Arg Arg Arg Ser Ser Gly Arg Val Ile Trp Asp Ser  
 1075 1080 1085  
 Trp Leu Pro Gly Phe Ala Phe Asn Asp Gln Phe Ile Gln Ile Ser Thr  
 1090 1095 1100  
 Arg Leu Pro Ser Glu Tyr Ile Tyr Gly Phe Gly Glu Val Glu His Thr  
 105 1110 1115 1120  
 20 Ala Phe Lys Arg Asp Leu Asn Trp Asn Thr Trp Gly Met Phe Thr Arg  
 1125 1130 1135  
 Asp Gln Pro Pro Gly Tyr Lys Leu Asn Ser Tyr Gly Phe His Pro Tyr  
 1140 1145 1150  
 Tyr Met Ala Leu Glu Glu Glu Gly Asn Ala His Gly Val Phe Leu Leu  
 1155 1160 1165  
 Asn Ser Asn Ala Met Asp Val Thr Phe Gln Pro Thr Pro Ala Leu Thr  
 1170 1175 1180  
 25 Tyr Arg Thr Val Gly Gly Ile Leu Asp Phe Tyr Met Phe Leu Gly Pro  
 185 1190 1195 1200  
 Thr Pro Gln Val Ala Thr Lys Gln Tyr His Glu Val Ile Gly His Pro  
 1205 1210 1215  
 Val Met Pro Ala Tyr Trp Ala Leu Gly Phe Gln Leu Cys Arg Tyr Gly  
 1220 1225 1230  
 Tyr Ala Asn Thr Ser Glu Val Arg Glu Leu Tyr Asp Ala Met Val Ala  
 1235 1240 1245  
 Ala Asn Ile Pro Tyr Asp Val Gln Tyr Thr Asp Ile Asp Tyr Met Glu  
 1250 1255 1260  
 30 Arg Gln Leu Asp Phe Thr Ile Gly Glu Ala Phe Gln Asp Leu Pro Gln  
 265 1270 1275 1280  
 Phe Val Asp Lys Ile Arg Gly Glu Gly Met Arg Tyr Ile Ile Ile Leu  
 1285 1290 1295  
 Asp Pro Ala Ile Ser Gly Asn Glu Thr Lys Thr Tyr Pro Ala Phe Glu  
 1300 1305 1310  
 Arg Gly Gln Gln Asn Asp Val Phe Val Lys Trp Pro Asn Thr Asn Asp  
 1315 1320 1325  
 35 Ile Cys Trp Ala Lys Val Trp Pro Asp Leu Pro Asn Ile Thr Ile Asp  
 1330 1335 1340  
 Lys Thr Leu Thr Glu Asp Glu Ala Val Asn Ala Ser Arg Ala His Val  
 345 1350 1355 1360  
 Ala Phe Pro Asp Phe Phe Arg Thr Ser Thr Ala Glu Trp Trp Ala Arg

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1365 1370 1375  
 Glu Ile Val Asp Phe Tyr Asn Glu Lys Met Lys Phe Asp Gly Leu Trp  
 1380 1385 1390  
 Ile Asp Met Asn Glu Pro Ser Ser Phe Val Asn Gly Thr Thr Asn  
 1395 1400 1405  
 Gln Cys Arg Asn Asp Glu Leu Asn Tyr Pro Pro Tyr Phe Pro Glu Leu  
 1410 1415 1420  
 5 Thr Lys Arg Thr Asp Gly Leu His Phe Arg Thr Ile Cys Met Glu Ala  
 425 1430 1435 1440  
 Glu Gln Ile Leu Ser Asp Gly Thr Ser Val Leu His Tyr Asp Val His  
 1445 1450 1455  
 Asn Leu Tyr Gly Trp Ser Gln Met Lys Pro Thr His Asp Ala Leu Gln  
 1460 1465 1470  
 Lys Thr Thr Gly Lys Arg Gly Ile Val Ile Ser Arg Ser Thr Tyr Pro  
 1475 1480 1485  
 Thr Ser Gly Arg Trp Gly Gly His Trp Leu Gly Asp Asn Tyr Ala Arg  
 1490 1495 1500  
 10 Trp Asp Asn Met Asp Lys Ser Ile Ile Gly Met Met Glu Phe Ser Leu  
 505 1510 1515 1520  
 Phe Gly Ile Ser Tyr Thr Gly Ala Asp Ile Cys Gly Phe Phe Asn Asn  
 1525 1530 1535  
 Ser Glu Tyr His Leu Cys Thr Arg Trp Met Gln Leu Gly Ala Phe Tyr  
 1540 1545 1550  
 Pro Tyr Ser Arg Asn His Asn Ile Ala Asn Thr Arg Arg Gln Asp Pro  
 1555 1560 1565  
 15 Ala Ser Trp Asn Glu Thr Phe Ala Glu Met Ser Arg Asn Ile Leu Asn  
 1570 1575 1580  
 Ile Arg Tyr Thr Leu Leu Pro Tyr Phe Tyr Thr Gln Met His Glu Ile  
 585 1590 1595 1600  
 His Ala Asn Gly Gly Thr Val Ile Arg Pro Leu Leu His Glu Phe Phe  
 1605 1610 1615  
 Asp Glu Lys Pro Thr Trp Asp Ile Phe Lys Gln Phe Leu Trp Gly Pro  
 1620 1625 1630  
 Ala Phe Met Val Thr Pro Val Leu Glu Pro Tyr Val Gln Thr Val Asn  
 1635 1640 1645  
 20 Ala Tyr Val Pro Asn Ala Arg Trp Phe Asp Tyr His Thr Gly Lys Asp  
 1650 1655 1660  
 Ile Gly Val Arg Gly Gln Phe Gln Thr Phe Asn Ala Ser Tyr Asp Thr  
 665 1670 1675 1680  
 Ile Asn Leu His Val Arg Gly Gly His Ile Leu Pro Cys Gln Glu Pro  
 1685 1690 1695  
 Ala Gln Asn Thr Phe Tyr Ser Arg Gln Lys His Met Lys Leu Ile Val  
 1700 1705 1710  
 25 Ala Ala Asp Asp Asn Gln Met Ala Gln Gly Ser Leu Phe Trp Asp Asp  
 1715 1720 1725  
 Gly Glu Ser Ile Asp Thr Tyr Glu Arg Asp Leu Tyr Leu Ser Val Gln  
 1730 1735 1740  
 Phe Asn Leu Asn Gln Thr Thr Leu Thr Ser Thr Ile Leu Lys Arg Gly  
 745 1750 1755 1760  
 Tyr Ile Asn Lys Ser Glu Thr Arg Leu Gly Ser Leu His Val Trp Gly  
 1765 1770 1775  
 Lys Gly Thr Thr Pro Val Asn Ala Val Thr Leu Thr Tyr Asn Gly Asn  
 1780 1785 1790  
 30 Lys Asn Ser Leu Pro Phe Asn Glu Asp Thr Thr Asn Met Ile Leu Arg  
 1795 1800 1805  
 Ile Asp Leu Thr Thr His Asn Val Thr Leu Glu Glu Pro Ile Glu Ile  
 1810 1815 1820  
 Asn Trp Ser  
 825

## (2) INFORMATION FOR SEQ ID NO:180:

35

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2284 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

B

CTT TTC ACA CTC CCT GGA ACT CCT ATA ACT TAC TAT GGA GAA GAA ATT 1496  
 Leu Phe Thr Leu Pro Gly Thr Pro Ile Thr Tyr Tyr Gly Glu Glu Ile  
 470 475 480

GGA ATG GGA AAT ATT GTA GCC GCA AAT CTC AAT GAA AGC TAT GAT ATT 1544  
 Gly Met Gly Asn Ile Val Ala Ala Asn Leu Asn Glu Ser Tyr Asp Ile  
 485 490 495 500

5 AAT ACC CTT CGC TCA AAG TCA CCA ATG CAG TGG GAC AAT AGT TCA AAT 1592  
 Asn Thr Leu Arg Ser Lys Ser Pro Met Gln Trp Asp Asn Ser Ser Asn  
 505 510 515

GCT GGT TTT TCT GAA GCT AGT AAC ACC TGG TTA CCT ACC AAT TCA GAT 1640  
 Ala Gly Phe Ser Glu Ala Ser Asn Thr Trp Leu Pro Thr Asn Ser Asp  
 520 525 530

10 TAC CAC ACT GTG AAT GTT GAT GTC CAA AAG ACT CAG CCC AGA TCG GCT 1688  
 Tyr His Thr Val Asn Val Asp Val Gln Lys Thr Gln Pro Arg Ser Ala  
 535 540 545

TTG AAG TTA TAT CAA GAT TTA AGT CTA CTT CAT GCC AAT GAG CTA CTC 1736  
 Leu Lys Leu Tyr Gln Asp Leu Ser Leu Leu His Ala Asn Glu Leu Leu  
 550 555 560

15 CTC AAC AGG GGC TGG TTT TGC CAT TTG AGG AAT GAC AGC CAC TAT GTT 1784  
 Leu Asn Arg Gly Trp Phe Cys His Leu Arg Asn Asp Ser His Tyr Val  
 565 570 575 580

GTG TAC ACA AGA GAG CTG GAT GGC ATC GAC AGA ATC TTT ATC GTG GTT 1832  
 Val Tyr Thr Arg Glu Leu Asp Gly Ile Asp Arg Ile Phe Ile Val Val  
 585 590 595

CTG AAT TTT GGA GAA TCA ACA CTG TTA AAT CTA CAT AAT ATG ATT TCG 1880  
 Leu Asn Phe Gly Glu Ser Thr Leu Leu Asn Leu His Asn Met Ile Ser  
 600 605 610

20 GGC CTT CCC GCT AAA ATA AGA ATA AGG TTA AGT ACC AAT TCT GCC GAC 1928  
 Gly Leu Pro Ala Lys Ile Arg Ile Arg Leu Ser Thr Asn Ser Ala Asp  
 615 620 625

AAA GGC AGT AAA GTT GAT ACA AGT GGC ATT TTT CTG GAC AAG GGA GAG 1976  
 Lys Gly Ser Lys Val Asp Thr Ser Gly Ile Phe Leu Asp Lys Gly Glu  
 630 635 640

25 GGA CTC ATC TTT GAA CAC AAC ACG AAG AAT CTC CTT CAT CGC CAA ACA 2024  
 Gly Leu Ile Phe Glu His Asn Thr Lys Asn Leu Leu His Arg Gln Thr  
 645 650 655 660

GCT TTC AGA GAT AGA TGC TTT GTT TCC AAT CGA GCA TGC TAT TCC AGT 2072  
 Ala Phe Arg Asp Arg Cys Phe Val Ser Asn Arg Ala Cys Tyr Ser Ser  
 665 670 675

30 GTA CTG AAC ATA CTG TAT ACC TCG TGT TAGGCACCTT TATGAAGAGA TGAAGAC 2126  
 Val Leu Asn Ile Leu Tyr Thr Ser Cys  
 680 685

ACTGGCATT T CAGTGGGATT GTAAGCATT GTAATAGCTT CATGTACAGC ATGCTGCTTG 2186  
 GTGAACAATC ATTAATTCTT CGATATTTCT GTAGCTTGAA TGTAACCGCT TTAAGAAAGG 2246  
 TTCTCAAATG TTTTGAAAAA AATAAAATGT TTAAGAGT 2284

(2) INFORMATION FOR SEQ ID NO:181:

35

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 685 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

B

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:181:

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5  Met Ala Glu Asp Lys Ser Lys Arg Asp Ser Ile Glu Met Ser Met Lys
   1      5      10      15
   Gly Cys Gln Thr Asn Asn Gly Phe Val His Asn Glu Asp Ile Leu Glu
   20      25      30
   Gln Thr Pro Asp Pro Gly Ser Ser Thr Asp Asn Leu Lys His Ser Thr
   35      40      45
   Arg Gly Ile Leu Gly Ser Gln Glu Pro Asp Phe Lys Gly Val Gln Pro
   50      55      60
   Tyr Ala Gly Met Pro Lys Glu Val Leu Phe Gln Phe Ser Gly Gln Ala
   65      70      75      80
10  Arg Tyr Arg Ile Pro Arg Glu Ile Leu Phe Trp Leu Thr Val Ala Ser
   85      90      95
   Val Leu Val Leu Ile Ala Ala Thr Ile Ala Ile Ile Ala Leu Ser Pro
   100     105     110
   Lys Cys Leu Asp Trp Trp Gln Glu Gly Pro Met Tyr Gln Ile Tyr Pro
   115     120     125
   Arg Ser Phe Lys Asp Ser Asn Lys Asp Gly Asn Gly Asp Leu Lys Gly
   130     135     140
15  Ile Gln Asp Lys Leu Asp Tyr Ile Thr Ala Leu Asn Ile Lys Thr Val
   145     150     155     160
   Trp Ile Thr Ser Phe Tyr Lys Ser Ser Leu Lys Asp Phe Arg Tyr Gly
   165     170     175
   Val Glu Asp Phe Arg Glu Val Asp Pro Ile Phe Gly Thr Met Glu Asp
   180     185     190
   Phe Glu Asn Leu Val Ala Ala Ile His Asp Lys Gly Leu Lys Leu Ile
   195     200     205
   Ile Asp Phe Ile Pro Asn His Thr Ser Asp Lys His Ile Trp Phe Gln
   210     215     220
20  Leu Ser Arg Thr Arg Thr Gly Lys Tyr Thr Asp Tyr Tyr Ile Trp His
   225     230     235
   Asp Cys Thr His Glu Asn Gly Lys Thr Ile Pro Pro Asn Asn Trp Leu
   245     250     255
   Ser Val Tyr Gly Asn Ser Ser Trp His Phe Asp Glu Val Arg Asn Gln
   260     265     270
   Cys Tyr Phe His Gln Phe Met Lys Glu Gln Pro Asp Leu Asn Phe Arg
   275     280     285
25  Asn Pro Asp Val Gln Glu Glu Ile Lys Glu Ile Leu Arg Phe Trp Leu
   290     295     300
   Thr Lys Gly Val Asp Gly Phe Ser Leu Asp Ala Val Lys Phe Leu Leu
   305     310     315     320
   Glu Ala Lys His Leu Arg Asp Glu Ile Gln Val Asn Lys Thr Gln Ile
   325     330     335
   Pro Asp Thr Val Thr Gln Tyr Ser Glu Leu Tyr His Asp Phe Thr Thr
   340     345     350
   Thr Gln Val Gly Met His Asp Ile Val Arg Ser Phe Arg Gln Thr Met
   355     360     365
30  Asp Gln Tyr Ser Thr Glu Pro Gly Arg Tyr Arg Phe Met Gly Thr Glu
   370     375     380
   Ala Tyr Ala Glu Ser Ile Asp Arg Thr Val Met Tyr Tyr Gly Leu Pro
   385     390     395     400
   Phe Ile Gln Glu Ala Asp Phe Pro Phe Asn Asn Tyr Leu Ser Met Leu
   405     410     415
   Asp Thr Val Ser Gly Asn Ser Val Tyr Glu Val Ile Thr Ser Trp Met
   420     425     430
35  Glu Asn Met Pro Glu Gly Lys Trp Pro Asn Trp Met Ile Gly Gly Pro
   435     440     445
   Asp Ser Ser Arg Leu Thr Ser Arg Leu Gly Asn Gln Tyr Val Asn Val
   450     455     460
   Met Asn Met Leu Leu Phe Thr Leu Pro Gly Thr Pro Ile Thr Tyr Tyr
   465     470     475     480

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[illegible]

30 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 19 amino acids  
 (B) TYPE: amino acid  
 (C) STRANDEDNESS:  
 (D) TOPOLOGY: unknown  
 (ii) MOLECULE TYPE: peptide  
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:183:

35 Ser Ala Arg Asp Ser Gly Pro Ala Glu Asp Gly Ser Arg Ala Val Arg  
 1 5 10 15  
 Leu Asn Gly

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WHAT IS CLAIMED IS:

1. A purified protein which specifically binds to a gastro-intestinal tract receptor selected from the group consisting of HPT1, hPEPT1, D2H, and hSI.

2. A protein which binds specifically to a gastro-intestinal transport receptor selected from the group consisting of HPT1, hPEPT1, D2H, and hSI, in which the protein comprises an amino acid sequence selected from the group consisting of SEQ ID NOS:1-55 or a binding portion thereof.

3. A protein which binds specifically to a gastro-intestinal transport receptor selected from the group consisting of HPT1, hPEPT1, D2H, and hSI, in which the amino acid sequence of the protein is selected from the group consisting of SEQ ID NOS:1-55, or a binding portion thereof.

4. The protein of claim 2 which comprises the amino acid sequence substantially as set forth in: SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 30, SEQ ID NO: 43, SEQ ID NO: 46, or SEQ ID NO: 52, or a binding portion thereof.

5. The protein of claim 3, the amino acid sequence of which consists of the amino acid sequence substantially as set forth in: SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 30, SEQ ID NO: 43, SEQ ID NO: 46, or SEQ ID NO: 52, or a binding portion thereof.

6. A protein of not more than 50 amino acids in length which specifically binds to a gastro-intestinal transport receptor selected from the group consisting of HPT1, hPEPT1, D2H, and hSI, in which the protein includes, positioned anywhere along its sequence, the contiguous amino

acid sequence of: Xaa<sub>1</sub> Thr Xaa<sub>2</sub> Xaa<sub>3</sub> Ser Xaa<sub>4</sub> Xaa<sub>5</sub> Xaa<sub>6</sub> Asn Xaa<sub>7</sub> Arg (SEQ ID NO:253), where Xaa<sub>1</sub> is Ser or Thr; Xaa<sub>2</sub> is Arg or Lys; Xaa<sub>3</sub> is Lys or Arg; Xaa<sub>4</sub> is Ser or Leu; Xaa<sub>5</sub> is Arg, Ile, Val, or Ser; Xaa<sub>6</sub> is Ser, Tyr, Phe, or His; and Xaa<sub>7</sub> is Pro, His or Arg.

7. The protein of claim 6 which is not more than 40 amino acids in length.

10 8. The protein of claim 6 which is not more than 30 amino acids in length.

9. The protein of claim 6 which is not more than 20 amino acids in length.

15

10. A protein of not more than 50 amino acids in length which specifically binds to a gastro-intestinal transport receptor selected from the group consisting of HPT1, hPEPT1, D2H, and hSI, in which the protein includes, 20 positioned anywhere along its sequence, the contiguous amino acid sequence of: Asp Xaa<sub>1</sub> Asp Xaa<sub>2</sub> Arg Arg Xaa<sub>3</sub> Xaa<sub>4</sub> (SEQ ID NO:254) where Xaa<sub>1</sub> is Ser, Ala, or Gly; Xaa<sub>2</sub> is Val or Gln; Xaa<sub>3</sub> is Pro, Gly, or Ser; and Xaa<sub>4</sub> is Trp or Tyr.

25 11. The protein of claim 10 which is not more than 40 amino acids in length.

12. The protein of claim 10 which is not more than 30 amino acids in length.

30

13. The protein of claim 10 which is not more than 20 amino acids in length.

14. A protein of not more than 50 amino acids in 35 length which specifically binds to a gastro-intestinal transport receptor selected from the group consisting of HPT1, hPEPT1, D2H, and hSI, in which the protein includes,

positioned anywhere along its sequence, the contiguous amino acid sequence of: Val Arg Ser Gly Cys Gly Xaa<sub>1</sub> Xaa<sub>2</sub> Ser Ser (SEQ ID NO:255), where Xaa<sub>1</sub> is Ala or Phe; and Xaa<sub>2</sub> is Arg or His.

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15. The protein of claim 14 which is not more than 40 amino acids in length.

16. The protein of claim 14 which is not more than 10 30 amino acids in length.

17. The protein of claim 14 which is not more than 20 amino acids in length.

15 18. A protein of not more than 50 amino acids in length which specifically binds to a gastro-intestinal transport receptor selected from the group consisting of HPT1, hPEPT1, D2H, and hSI, in which the protein includes, positioned anywhere along its sequence, the contiguous amino  
20 acid sequence of: NTRKSSRSNPR (SEQ ID NO:256) or STKRSLIYNHR (SEQ ID NO:257) or STGRKVFNRR (SEQ ID NO:258) or TNAKHSSHNR (SEQ ID NO:259).

19. A protein of not more than 50 amino acids in  
25 length which specifically binds to a gastro-intestinal transport receptor selected from the group consisting of HPT1, hPEPT1, D2H, and hSI, in which the protein includes, positioned anywhere along its sequence, the contiguous amino acid sequence of: DSDVRRPW (SEQ ID NO:260) or AADQRRGW (SEQ  
30 ID NO:261) or DGRGGRSY (SEQ ID NO:262).

20. A protein of not more than 50 amino acids in length which specifically binds to a gastro-intestinal transport receptor selected from the group consisting of  
35 HPT1, hPEPT1, D2H, and hSI, in which the protein includes, positioned anywhere along its sequence, the contiguous amino

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acid sequence of: RVRS (SEQ ID NO:263) or SVRSGCGFRGSS (SEQ ID NO:264) or SVRGGCGAHSS (SEQ ID NO:265).

21. The protein of claim 1, 2, 3, 6, 10, 14, 18, 5 19, or 20 which is purified.

22. A composition comprising the protein of claim 1, 2, 3, 6, 10, 14, 18, 19, or 20, bound to a material comprising an active agent, said active agent being of value 10 in the treatment of a mammalian disease or disorder.

23. The composition of claim 22 in which the active agent is a drug.

15 24. The composition of claim 22 in which the material is a particle containing the active agent.

25. The composition of claim 22 in which the material is a slow-release device containing the drug.

20

26. The composition of claim 22 in which the protein is covalently or noncovalently bound to the material.

27. A composition comprising a chimeric protein 25 bound to a material comprising an active agent, in which the chimeric protein comprises a sequence selected from the group consisting of SEQ ID NOS:1-55 or a binding portion thereof fused via a covalent bond to an amino acid sequence of a second protein, in which the active agent is of value in the 30 treatment of a mammalian disease or disorder.

28. A composition comprising the protein of claim 1, 2, 3, 6, 10, 14, 18, 19, or 20 covalently bound to a particle containing a drug.

35

29. A composition comprising the protein of claim 1, 2, 3, 6, 10, 14, 18, 19, or 20 covalently bound to a drug.